## Health Care Provider Hemoglobinopathy Fact Sheet

# Hemoglobin Bart's & Alpha Thalassemia

Hemoglobin Bart's is a tetramer of gamma (fetal) globin chains seen during the newborn period. Its presence indicates that one or more of the four genes that produce alpha globin chains is dysfunctional, causing alpha thalassemia. The more alpha genes affected, the more significant the thalassemia and clinical symptoms. Alpha thalassemia occurs in individuals of all ethnic backgrounds and is one of the most common genetic diseases worldwide. However, the clinically significant forms (Hemoglobin H disease and Alpha Thalassemia Major) occur predominantly among Southeast Asians. Summarized below are the manifestations of different numbers of affected alpha globin genes and recommendations for follow-up of Hemoglobin Bart's.

**Silent Carrier - ONE** dysfunctional alpha gene:
If one alpha gene is affected, the other three genes can compensate nearly completely. These individuals are clinically and hematologically normal. Follow-up is for the sole benefit of determining reproductive risks for the family.

**Alpha Thalassemia Trait - TWO** dysfunctional genes:
Dysfunction of two alpha genes results in a mild anemia with microcytosis. This is benign and requires no treatment. Follow-up is for the benefit of avoiding mis-diagnosis of iron deficiency, or diagnostic dilemmas of non-responsive anemia. It is also for the benefit of determining reproductive risks for the family, which will differ depending on whether the two dysfunctional genes are on the same or different allele of chromosome number 16 (cis and trans pattern respectively).

**Hemoglobin H Disease - THREE** dysfunctional genes:
Three dysfunctional alpha genes generally result in a moderate hemolytic anemia. This usually occurs when one parent is a silent carrier (one dysfunctional alpha gene) and the other has alpha thalassemia trait (two dysfunctional alpha genes) in a cis pattern. The clinical manifestations of this disorder are variable but most patients are anemic and develop some degree of splenomegaly. Hemoglobin H is unstable and patients with hemoglobin H disease have chronic hemolysis in addition to alpha thalassemia. They are susceptible to accelerated hemolysis when exposed to the same drugs that cause hemolysis in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency. A list of these drugs can be furnished on request.

**Alpha Thalassemia Major** (Fetal Hydrops Syndrome) - **FOUR** (all) genes dysfunctional:
If none of the alpha genes are functional, a very severe hemolytic anemia begins in utero. The anemia is so severe that the disorder is lethal with fetal demise usually occurring in the third trimester. Also, pregnant women carrying an infant with fetal hydrops syndrome have a high rate of severe toxemia of pregnancy. This usually occurs when both parents have alpha thalassemia trait in the cis pattern. Prospective parent screening and intrauterine diagnosis are appropriate if the potential for fetal hydrops syndrome is suspected.

---

*Genetic counseling is advisable for families affected by these conditions to promote understanding of the significance for themselves and future offspring. A list of genetic counselors and hemoglobin consultants was included with this fact sheet* ***(additional copies are available from our office, see reverse of this page).***

# Follow-up of Newborns with Hemoglobin Bart's

The following recommendations were developed with the help of the Newborn Screening Program's Hematology Consultants.

## At Two to Three Months

**Examine baby for splenomegaly and do a complete blood count (CBC).**

- If both are normal, and no other hemoglobin abnormality other than Hemoglobin Bart's was present at birth, Hemoglobin H disease is unlikely and no further work-up is necessary until 9 to 12 months.

- If either is abnormal, the infant is at risk of developing Hemoglobin H disease. Consultation with an expert in the assessment of these abnormalities is recommended.

## Between Nine and Twelve Months

**Do a CBC and reticulocytes.**

- If results are normal, the child most likely is a silent carrier and the family is not at risk for Fetal Hydrops Syndrome in future pregnancies. No further work-up is necessary.

- If microcytic, do iron studies:

  If iron-deficient, treat for 3 to 6 months then repeat the CBC. If microcytosis is corrected, the child most likely is a silent carrier and the family is not at risk for Fetal Hydrops Syndrome in a future pregnancy. No further work-up is necessary.

  If not iron deficient, (or if microcytosis persists after iron deficiency has been corrected), do a hemoglobin electrophoresis or HPLC (including quantitation of hemoglobins A2 and F). The work-up should include a stain for hemoglobin H inclusion bodies using brilliant cresyl blue. High levels of hemoglobin H inclusion bodies and unresolved microcytic anemia, indicate that the child has Hemoglobin H disease. Lower levels of inclusion bodies are found with alpha thalassemia trait. Consultation with an expert in the assessment of these abnormalities is recommended.

Upon completion of the above, please return the enclosed **Diagnostic Evaluation Form**. This information enables us to assess the correlation of the level of Hemoglobin Bart's on the newborn screening test with the clinical form of Alpha Thalassemia.

*The parents of a child with Hemoglobin Bart's, especially if at least one parent is Asian, should also have a CBC. If either parent is microcytic, further evaluation of the parents for alpha thalassemia may be warranted due to the risk of Hemoglobin H Disease or Alpha Thalassemia Major in future children.*

Washington State Department of Health • Newborn Screening Program
1610 NE 150th Street, K17-9 • Shoreline, WA 98155-0729 • www.doh.wa.gov/nbs
Phone: (206) 418-5410 • FAX: (206) 418-5415 • E-mail: NBS.Prog@doh.wa.gov

Revised 3/05